

WHAT IS CLAIMED IS:

1. An antibody or an active fragment or derivative thereof specific for a RAP-2 (RIP associated protein-2) protein whose sequence is that of SEQ ID NO:4, or an analog of SEQ ID NO:4 which differs therefrom by no more than ten changes in the amino acid sequence thereof, each said change being a substitution, deletion and/or insertion of a single amino acid, which analog is capable of binding to RIP.

2. A method for the modulation or mediation of the RIP modulated/mediated intracellular effects on the inflammation, cell death or cell survival pathways in which RIP is involved directly, or indirectly via other modulators/mediators of these pathways, comprising treating said cells with a polypeptide that is capable of binding to RIP and modulating or mediating said intracellular activity of RIP, wherein said treating of said cells comprises introducing into said cells said polypeptide in a form suitable for intracellular introduction thereof, or introducing into said cells a DNA sequence encoding said polypeptide in the form of a suitable vector carrying said sequence, said vector being capable of effecting the insertion of said sequence into said cells in a way that said sequence is expressed in said cells, wherein said polypeptide has the amino acid sequence of:

(a) a RAP-2 (RIP-associated protein-2) protein whose sequence is that of SEQ ID NO:4;

(b) a fragment of (a) which is capable of binding to RIP;

(c) an analog of (a) which differs from the sequence of (a) by no more than ten changes in the amino acid sequence of (a), each said change being a substitution, deletion and/or insertion of a single amino acid, which analog is capable of binding to RIP; or

(d) a derivative of (a), (b) or (c) by modification of a functional group which occurs as a side chain or an N- or C-terminal group of one or more amino acid residues thereof without changing one amino acid to another of the twenty commonly occurring natural amino acids, which derivative is capable of binding to RIP.

3. A method for the modulation of the RIP modulated/mediated effect on cells according to claim 2, wherein said treating of cells comprises introducing into said cells a DNA sequence encoding said polypeptide in the form of a suitable vector carrying said sequence, said vector being capable of effecting the insertion of said sequence into said cells in a way that said sequence is expressed in said cells.

4. A method according to claim 2 wherein said treating of said cells is by transfection of said cells with a recombinant animal virus vector comprising the steps of:

(a) constructing a recombinant animal virus vector carrying a sequence encoding a viral surface protein (ligand) that is capable of binding to a specific cell surface receptor on the surface of said cells to be treated and a second sequence encoding said polypeptide; and

(b) infecting said cells with said vector of (a).

5. A method for modulating RIP modulated/mediated effect on cells comprising treating said cells with antibodies or active fragments or derivatives thereof, according to claim 1, said treating being by application of a suitable composition containing said antibodies, active fragments or derivatives thereof to said cells, wherein when the RAP-2 protein or portions thereof of said cells are exposed on the extracellular surface, said composition is formulated for extracellular application, and when said RAP-2 proteins are intracellular said composition is formulated for intracellular application.

6. An antisense oligonucleotide consisting of a sequence complementary to at least a portion of the mRNA encoding a polypeptide comprising the amino acid sequence of residues 1-416 of SEQ ID NO:4.

7. A method for modulating the RIP modulated/mediated effect on cells comprising treating said cells with an antisense oligonucleotide according to claim 6, said antisense oligonucleotide being capable of blocking the expression of the RAP-2 protein.

8. A method according to claim 7, wherein said antisense oligonucleotide is introduced to said cells by transfection of said cells with a recombinant animal virus vector comprising the steps of:

(a) constructing a recombinant animal virus vector carrying a sequence encoding a viral surface protein (ligand) that is capable of binding to a specific cell surface receptor on the surface of said cells to be treated and a second sequence consisting of said antisense oligonucleotide; and

(b) infecting said cells with said vector of (a).

9. A method for treating tumor cells or HIV-infected cells or other diseased cells, comprising:

(i) constructing a recombinant animal virus vector carrying a sequence encoding a viral surface protein capable of binding to a specific tumor cell surface receptor or HIV-infected cell surface receptor or receptor carried by other diseased cells and a sequence encoding a polypeptide that is capable of binding to RIP, that when expressed in said tumor, HIV-infected, or other diseased cell is capable of enhancing

the RIP modulated/mediated direct or indirect killing of said cell, wherein said polypeptide has the amino acid sequence of:

(a) a RAP-2 (RIP-associated protein-2) protein whose sequence is that of SEQ ID NO:4;

(b) a fragment of (a) which is capable of binding to RIP;

(c) an analog of (a) which differs from the sequence of (a) by no more than ten changes in the amino acid sequence of (a), each said change being a substitution, deletion and/or insertion of a single amino acid, which analog is capable of binding to RIP; or

(d) a derivative of (a), (b) or (c) by modification of a functional group which occurs as a side chain or an N- or C-terminal group of one or more amino acid residues thereof without changing one amino acid to another of the twenty commonly occurring natural amino acids, which derivative is capable of binding to RIP.; and

(ii) infecting said tumor or HIV-infected cells or other diseased cells with said vector of (i).

10. A method for modulating the RIP effect on cells comprising applying the ribozyme procedure in which a vector encoding a ribozyme sequence capable of interacting with a

cellular mRNA sequence encoding a polypeptide comprising the amino acid sequence of residues 1-416 of SEQ ID NO:4, is introduced into said cells in a form that permits expression of said ribozyme sequence in said cells, and wherein when said ribozyme sequence is expressed in said cells it interacts with said cellular mRNA sequence and cleaves said mRNA sequence resulting in the inhibition of expression of said RAP-2 protein in said cells.

11. A pharmaceutical composition for modulating the RIP effect on cells comprising as active ingredient, an antisense oligonucleotide according to claim 6.

12. A method of modulating processes modulated/mediated by RIP directly or indirectly comprising treating cells with a polypeptide that is capable of binding to RIP, wherein said treating of said cells comprises introducing into said cells said polypeptide in a form suitable for intracellular introduction thereof, or introducing into said cells a DNA sequence encoding said polypeptide in the form of a suitable vector carrying said sequence, said vector being capable of effecting the insertion of said sequence into said cells in a way that said sequence is expressed in said cells, wherein said polypeptide has the amino acid sequence of:

(a) a RAP-2 (RIP-associated protein-2) protein whose sequence is that of SEQ ID NO:4;

(b) a fragment of (a) which is capable of binding to RIP;

(c) an analog of (a) which differs from the sequence of (a) by no more than ten changes in the amino acid sequence of (a), each said change being a substitution, deletion and/or insertion of a single amino acid, which analog is capable of binding to RIP; or

(d) a derivative of (a), (b) or (c) by modification of a functional group which occurs as a side chain or an N- or C-terminal group of one or more amino acid residues thereof without changing one amino acid to another of the twenty commonly occurring natural amino acids, which derivative is capable of binding to RIP.

13. A method of modulating processes that are mediated/modulated by RIP directly or indirectly and which include the inhibition of NF-KB, and activation of JNK and p38 kinase, comprising treating cells a polypeptide that is capable of binding to RIP, wherein said treating of cells comprises introducing into said cells said polypeptide in a form suitable for intracellular introduction thereof, or introducing into said cells a DNA sequence encoding said polypeptide in the form of a suitable vector carrying said

sequence, said vector being capable of effecting the insertion of said sequence into said cells in a way that said sequence is expressed in said cells, wherein said polypeptide has the amino acid sequence of:

(a) a RAP-2 (RIP-associated protein-2) protein whose sequence is that of SEQ ID NO:4;

(b) a fragment of (a) which is capable of binding to RIP;

(c) an analog of (a) which differs from the sequence of (a) by no more than ten changes in the amino acid sequence of (a), each said change being a substitution, deletion and/or insertion of a single amino acid, which analog is capable of binding to RIP; or

(d) a derivative of (a), (b) or (c) by modification of a functional group which occurs as a side chain or an N- or C-terminal group of one or more amino acid residues thereof without changing one amino acid to another of the twenty commonly occurring natural amino acids, which derivative is capable of binding to RIP.

14. A method for isolating and identifying proteins capable of binding to RAP-2 (SEQ ID NO:4), comprising applying the yeast two-hybrid procedure in which a sequence encoding said RAP-2 is carried by one hybrid vector and sequence from a cDNA or genomic DNA library is carried by the second hybrid



vector, the vectors then being used to transform yeast host cells and the positive transformed cells being isolated, followed by extraction of the said second hybrid vector to obtain a sequence encoding a protein which binds to said RAP-2.

15. A method of modulating/mediating the function of RAP-2, comprising treating cells with a RAP-2 binding protein, isolated and identified by the process of claim 14.

16. A method of modulating/mediating the function of RAP-2, comprising treating cells with a RAP-2 binding protein encoded by clone 10 or CGR 19.